STATE OF MICHIGAN
IN THE MICHIGAN SUPREME COURT

(On Appeal from the Michigan Court of Appeals and the Circuit Court for the County of Eaton)

TERI WALTERS and KIM WALTERS

Plaintiffs-Appellees,

v

DONALD S. FALIK d/b/a FALIK FAMILY DENTISTRY; DONALD S. FALIK, D.D.S.; ROBERT C. FALIK, D.D.S. and JANE DOE, jointly and severally

Defendants-Appellants.

_____/

Sup. Ct. No. 154489
COA No. 319016
Trial Court No: 12-658-NH

DEFENDANTS-APPELLANTS' REPLY BRIEF IN SUPPORT OF APPLICATION FOR LEAVE TO APPEAL

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STATEMENT OF ISSUE

DID THE CIRCUIT COURT ACT WITHIN THE PROPER EXERCISE OF ITS DISCRETION IN STRIKING THE TESTIMONY OF PLAINTIFFS' MEDICAL CAUSATION EXPERT UNDER MRE 702 and MCL 600.2955 WHERE THE COURT CLOSELY SCRUTINIZED THE SUBSTANCE AND SCIENTIFIC BASIS OF THE EXPERT OPINION AND FOUND THE OPINION TO BE UNSUPPORTED BY ANY RELIABLE SCIENTIFIC PRINCIPLES OR METHODS - - INCLUDING THE COMPLETE ABSENCE OF AN ASSOCIATION BETWEEN PHOSPHORIC ACID AND WG?

The Circuit Court said: Yes

The Court of Appeals said: No

Plaintiffs-Appellees say: No

Defendants-Appellants say: Yes

REPLY ARGUMENT

THE CIRCUIT COURT ACTED WITHIN THE PROPER EXERCISE OF ITS DISCRETION IN STRIKING THE TESTIMONY OF PLAINTIFF'S MEDICAL CAUSATION EXPERT UNDER MCL 600.2955(1) AND MRE 702 WHERE THE COURT CLOSELY SCRUTINIZED THE SUBSTANCE AND SCIENTIFIC BASIS OF THE OPINION AND FOUND THE OPINION TO BE UNSUPPORTED BY ANY RELIABLE SCIENTIFIC PRINCIPLES OR METHODS.

A. The Court of Appeals Erroneously Applied a *De Novo* Standard of Review, As Now Admitted by Plaintiffs.

To re-emphasize, the proper standard of review is that of an "abuse of discretion."

On the issue of the proper exercise of the trial court's "gatekeeper function" an abuse of discretion "occurs when the trial court chooses an outcome falling outside the range of principled outcomes." *Edry v Adelman*, 486 Mich 634, 639: 786 NW 2d 567 (2010).

The Court of Appeals' majority opinion on remand cited to the "abuse of discretion" standard of review, but effectively engaged in its own de facto, de novo review of the trial court's analysis. Significantly, Plaintiff's themselves recognize this controlling fact, stating in their current brief : "The COA rejected the Circuit's[sic] misapplication of MRE 702 and MCL 600.2955(1) **upon *de novo* review…**"(Appellees' Response to Application for Leave to Appeal, p. 2).

The Court of Appeals' majority's *de facto* employment of a *de novo* standard of review was palpably and reversibly erroneous. The text of the Court of Appeals' majority opinion does not explicitly demonstrate that the majority weighed whether the trial court's ruling fell "outside the range of reasonable and principled outcomes," *Elher v Misra*, 499 Mich 11; 878 NW 2d 790 (2016), or was "so palpably and grossly violative of fact and logic that it evidences perversity of will or the exercise of passion or bias rather than the exercise of discretion." *Maldonado v Ford Motor Co*, 476 Mich 372, 388, 719 NW2d 809 (2006). Rather, the Court of

Appeals majority opinion reads as if the panel erroneously conducted its own *de novo* balancing of factors. That Plaintiffs themselves recognize this enhances the need for affirmative Supreme Court action.

B. The Michigan Supreme Court Nor The Legislature Have Yet To Recognize The Validity Of The Sir Bradford Hill Criteria Of Causation In Michigan, Especially Absent Scientific Studies Supporting The Association Between A Specific Agent And The Subject Disease

The Defendants' Application for Leave to Appeal presents a clearly defined issue of significance to the jurisprudence of the state: whether the Sir Bradford Hill criteria of causation may be used as a substitute for all the other controlling criteria of scientific reliability set forth by the Michigan Supreme Court and Michigan legislature where: (1) the governing statute does not authorize the substitution and (2), in other jurisdictions, the Sir Bradford Hill criteria may not be used as an appropriate methodology by an epidemiologist to establish medical causation unless there is first a showing of the existence of independent data from controlled studies demonstrating an association between the agent and the medical condition. See, e.g., *In re Fosamax Prods Liab Litigation*, 645 F Supp 2d 164, 188 (SD NY 2009). Defendants assert that -- contrary to the ruling of the Court of Appeals' majority opinion -- the trial court acted within a proper exercise of its discretion in excluding the subject testimony because Plaintiff failed to make such a threshold showing of "association" in the trial court [as articulated by both the trial court and the Court of Appeals' dissenting opinions both before and, by incorporation, after the initial remand].

The insufficiency of Plaintiff's proofs and error of the Court of Appeals' majority are analogous to the inadequacy of the proffered expert's proofs found in *Frischhertz v Smithkline Beacham Corp*, 2012 US Dist LEXIS 181507 (ED La 2012) (attached hereto as Exhibit A). As

equally applicable here, the Court there explained:

> Dr. Goldstein's causation analysis also did not meet the required level for peer review or the standard that is accepted in his professional community, and he appears to have inappropriately applied the Bradford-Hill criteria for both general and specific causation. The Bradford-Hill criteria can only be applied after a statistically significant association has been identified. Federal Judicial Center, Reference Manual on Scientific Evidence, 599, n.141 (3d. ed. 2011) ("In a number of cases, experts attempted to use these guidelines to support the existence of causation in the absence of any epidemiologic studies finding an association . . . . There may be some logic to that effort, but it does not reflect accepted epidemiologic methodology."). See, e.g., Dunn v Sandoz Pharms., 275 F. Supp. 2d 672, 678 (M.D.N.C. 2003). Here, Dr. Goldstein attempted to use the Bradford-Hill criteria to prove causation without first identifying a valid statistically significant association. **He first developed a hypothesis and then attempted to use the Bradford-Hill criteria to prove it.** Rec. Doc. 187, Exh. 2, depo. Goldstein, p. 103. Because there is no data showing an association between Paxil and limb defects, no association existed for Dr. Goldstein to apply the Bradford-Hill criteria. Hence, Dr. Goldstein's general causation opinion is not reliable.
>
> Exhibit A, ** 9-10 [emphasis added]

In their current response here, Plaintiffs attempt to argue that the applicability of the Bradford Hill criteria to this action was sufficiently established by the testimony of the expert witness (Dr. Gershwin) and supporting articles which satisfy the criteria necessary to render his opinion "reliable." However, as was recognized by the Court of Appeals dissenting opinion below, Plaintiffs do not produce a single article, peer-reviewed study or any other scientific support for Dr. Gershwin's novel theory that etching solution or *phosphoric acid* is associated with, causes, or in any way contributes to Wegener's Granulomatosis. (See exhibits 18-42, 44, 45 attached to Plaintiffs' brief) None of these articles supports Dr. Gershwin's theory; in fact, even these articles contradict each other on suspected causes of Wegener's Granulomatosis.

The many articles attached to Plaintiffs' brief suggest there have been studies performed on mice and rats to test various substances possibly linked to Wegener's Granulomatosis, including staph aureus bacteria as indicated previously. Further, the articles describe several

studies that have been done retrospectively to examine a possible association with phosphates silica dust, farming, certain industrial solutions, etc. The overwhelming results of the many studies outlined in the articles are that there has been some moderate link hypothesized to staph aureus bacteria, a minimal link at best to silica dust, and even less to farming and other environmental causes like industrial solutions. **(See exhibits 18-42, 44, 45 attached to Plaintiffs' brief; none of the articles support Dr. Gershwin's theory).** There has never been any link, not even one case, to etching solution or phosphoric acid in any diagnosed case of Wegener's or any other vasculitis of any kind.

In the present case, the trial court properly concluded that not a single article, peer-reviewed study or any other scientific support was produced by Plaintiff to substantiate Dr. Gershwin's novel theory that etching solution or phosphoric acid causes, contributes to, or in any way sparks Wegener's Granulomatosis. (Exhibit A to Application, pp 20-21, 24-29). The trial court's order was not an abuse of discretion because this absence of scientific data associating etching solution or phosphoric acid with WG renders Dr. Gershwin's reliance on the Bradford Hill criteria palpably erroneous as a matter of law. *Frischhertz*, supra.

C. Speculative Analogy Does Not Substitute For Reliable Proof

In law, whether malpractice or general negligence, plaintiffs are required demonstrate proof by facts and reliable expert testimony, not speculation by analogy. When medicine is at issue, those proofs must be supported by reliable scientific data. *Craig v Oakwood Hosp*, 471 Mich 67; 684 NW2d 296 (2004). Proof of medical causation by the Bradford Hill criteria should not substitute "analogy" or speculative connections in place of independent evidence of direct association and, then, cause and effect.

Upon reading all of the studies proffered by Plaintiffs, one item is glaringly missing--any mention **of phosphoric acid** or dental solution causing or having any association to WG. Indeed, in their brief, Plaintiffs insufficiently rely upon speculative "analogy" to other tested agents, including the similarly worded but distinct agent "phosphates":

> "Dr. Gershwin explained that scientific principles of analogy and the mechanism by which WG is triggered permit data and principles derived from peer-reviewed analysis and epidemiological studies of various chemicals to be analogized in determining if exposure to phosphoric acid etching solution, a highly potent electrophilic solution could lead to the onset of WG here."
>
> Plaintiffs' Response Brief, p. 27.

Plaintiffs cite to journal articles -- Exhibits 18, 19, 20, 22, 24, 25, 26, 30, 31, 32, 33, 36, 37, 38, 39, 40, 41, and 42 to their brief -- as evidence of relevant analogies. None of those articles conclude that exposure to phosphoric acid, etching solution, or phosphorus is in any way associated with the onset of Wegener's Granulomatosis. Allowing such evidence by analogy, rather than by fact, to be presented to a jury when the scientific community considers the etiology of Wegener's to be "unknown" is clear error. In fact, again reviewing the myriad of studies and data available, the analysis of the etiology of Wegener's is summed up as follows in Plaintiffs' own Exhibit:

> Analytic investigations suggest several potential contributors to the development of WG, including various genetic polymorphisms, a possible association with crystalline silica exposure and more preliminary links with other environmental factors. Thus, for any of the observed associations, it is presently unclear whether they reflect causality or whether they are modifiers of disease expression or merely confounders.

See Plaintiffs' Exhibit 18, Epidemiology of Wegener's Granulomatosis: Lessons From Descriptive Studies And Analyses Of Genetic And Environmental Risk Determinants, Clin Exp Rheumatol 2006; 24 (Suppl. 41) S82-S91 [emphasis added]. Even looking at all of the data available, the attached "review" by experts at The Section of Rheumatology and the Clinical

Epidemiology Unit, Boston University School of Medicine, could only loosely observe that crystalline silica may be a "possible" environmental contributor to Wegener's Granulomatosis, but found no other factor that was even specifically mentionable in the review. *Id.* There were no conclusions regarding similar solutions, related chemical compositions, or other substances subject to Plaintiffs' analogies.

Similarly, Exhibit 19 contradicts Plaintiffs' position regarding staph aureus, stating that staph aureus nasal infection is *not* a possible cause of WG, but only a symptom of the disease.

Thus, when asked about whether there are any studies or other data which support a link between phosphoric acid or dental etching solution to Wegener's, Plaintiffs-Appellees' expert simply deflected the questions and resorted to analogies. A key example question is:

> Q. Do any of the literature pieces that you provided conclude that phosphoric acid causes or contributes to Wegener's?
>
> A. Well, again, the use of your words, the exact choice of your words would be no. But on the other hand, there is data about solvents, hydrocarbons, and agriculture. And I remind people that phosphorous and the element Si, silica, are adjacent to each other in the table of different chemicals. Remember what the periodic table is? . . .
>
> (Exhibit B to Application, p. 22).

In their current response, Plaintiffs attack the trial court's ruling as not recognizing the authority which links phosphates (but not phosphoric acid) as associated with the onset of WG. This echoes the analysis of the Court of Appeals majority opinion. However, as explained in the Defendant's current Application, phosphate and phosphoric acid contain common but not the completely same elements.

It was up to the trial court to determine if the analogies were sufficiently similar to serve as reliable supporting data under the statutory criteria or the Sir Bradford Hill criteria, if adopted in the place of the statutory factors. In this vein, **the trial court found that the**

additional "analogies" proffered by Plaintiffs were overstated and were too speculative to serve as reliable, scientific "proof" of anything (see: Exhibit A to Defendants' Application, p. 21, 24-25, 28-29). Plaintiffs repeat these overly broad and otherwise inaccurate factual misstatements in their current response brief regarding the sufficiency of purported *similarities* of tested chemicals such as phosphates to phosphoric acid and the alleged strength of the association between these other elements and WG. The Supreme Court should not be persuaded by these tactics.

D. Other Portions of Dr. Gershwin's Opinion Do Not Support the Opinion's Reliability Regarding Causation

Plaintiffs point to other portions of Dr. Gershwin's opinion as being independent data which purportedly supports the opinion's reliability. For example, Plaintiffs cite to the facts that WG requires a rare genetic predisposition and involve inflammation of the upper airways, which plaintiff had. These facts may support that Plaintiff suffered from WG. But, they don't establish causation and certainly do not constitute the independent data necessary to support application of the Sir Bradford Hill criteria. Likewise, the fact that experimental testing on live patients would be unethical may explain the difficulties in developing the independent data; but, they do not excuse the absence of that data.

CONCLUSION

The trial court's order was not an abuse of discretion. It should be reinstated by the Supreme Court.

Defendants-Appellants respectfully request this Honorable Court grant leave to appeal or peremptorily vacate the Court of Appeals opinion and affirm the order of the Eaton County Circuit Court striking Dr. Gershwin's testimony from consideration in this case.

Respectfully submitted,

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EXHIBIT A

Frischhertz v. SmithKline Beecham Corp.

United States District Court for the Eastern District of Louisiana

December 21, 2012, Decided; December 21, 2012, Filed

CIVIL ACTION NO. 10-2125 SECTION "C"(4)

Reporter
2012 U.S. Dist. LEXIS 181507; 90 Fed. R. Evid. Serv. (Callaghan) 328; 2012 WL 6697124

ANDREA FRISCHHERTZ, wife of/and BRAD FRISCHHERTZ, individually and on behalf of the minor child, E.F. versus SMITHKLINE BEECHAM CORPORATION d/b/a GLAXOSMITHKLINE

Subsequent History: Costs and fees proceeding at, Motion granted by *Frischhertz v. Smithkline Beechan Corp, 2013 U.S. Dist. LEXIS 104976 (E.D. La., July 26, 2013)*

Prior History: *Frischhertz v. Smithkline Beecham Corp., 2012 U.S. Dist. LEXIS 100139 (E.D. La., July 19, 2012)*

Core Terms

causation, summary judgment, scientific, limb, motion to exclude, reliability, serotonin, depo, plaintiffs', toxicology, pregnancy, defects, birth defect, heart defect, epidemiologic, admissible, teratogen, genuine

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Judges: HELEN G. BERRIGAN, UNITED STATES DISTRICT JUDGE.

Opinion by: HELEN G. BERRIGAN

Opinion

ORDER & REASONS

Before the Court are six motions: (1) Defendant GlaxoSmithkline LLC's Motion to Exclude the Testimony of Susan R. Andrews, Ph.D. Rec. Doc. 185; (2) Defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Joseph A. Hirsch, Ph.D. Rec. Doc. 186; (3) Defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Paul Goldstein, Ph.D. Rec. Doc. 187; (4) Defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Shira Kramer. Rec. Doc. 188; (5) Defendant GlaxoSmithKline LLC's Motion to Strike the Testimony of Edward J. Trapido, Sc.D. Rec. Doc. 190; and (5) Defendant GlaxoSmithKline LLC's Renewed Motion for Summary Judgment. Rec. Doc. 233. On October 3, 2012, the Court held a *Daubert* hearing where oral argument was heard on motions (3) through (5). Rec. Doc. 229. The plaintiffs and defendant also filed post-hearing briefs. Rec. Docs. 245, 246. The most significant motions in terms of impact upon the case are Rec. Doc. 187 and Rec. Doc. 188 concerning the testimony of Paul Goldstein, Ph.D. and Shira Kramer, Ph.D. [*3] and Rec. Doc. 233, the defendant's renewed motion for summary judgment. For that reason the Court will address these only.

1. Defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Paul Goldstein, Ph.D. is GRANTED. Rec. Doc. 187

2. Defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Shira Kramer is GRANTED. Rec. Doc. 188.

3. Defendant GlaxoSmithKline LLC's Renewed Motion for Summary Judgment is GRANTED. Rec. Doc. 233.

Plaintiffs Andrea Frischhertz and her husband Brad Frischhertz bring this claim on behalf of their son, E.F., a minor (hereinafter collectively "plaintiffs") against GlaxoSmithKline ("GSK"), the manufacturer of Paxil. Plaintiffs concede that their only claim remaining is for inadequate warning under the Louisiana Products Liability Act ("LPLA"). Rec. Doc. 139, p.1., n.1.

I. BACKGROUND

The petition for damages alleges that plaintiff, Andrea Frischhertz, took Paxil as prescribed by her doctor while she was pregnant with E.F. Rec. Doc.1. Paxil is a Selective Serotonin Reuptake Inhibitor (SSRI) commonly prescribed to treat depression. As a result of the medication, the petition for damages and the first amended and supplemental complaint allege that E.F. [*4] was born with "incomplete development of the cardiac septum, and irreversible birth defects" including cardiac deformities and Holt-Oram Syndrome. (Rec. Doc. 64). Holt-Oram Syndrome is a heart-hand syndrome that is characterized by hand abnormalities and an atrial septal defect. The defendant contests whether E.F. has this syndrome. The parties agree that E.F. has a limb abnormality that makes his fingers on his right hand smaller than his left. E.F. was born March 30, 2005. Plaintiffs allege that GSK had knowledge that Paxil caused birth defects while taken during pregnancy before Mrs. Frischhertz took the medication during her pregnancy with E.F. but did not release this information until September 2005.

II. LEGAL STANDARDS FOR ADMISSIBILITY- *DAUBERT*

The United States Supreme Court revised the standards for admitting scientific evidence under the Federal Rules of Evidence in *Daubert v. Merrell Dow Pharmaceuticals Inc., 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993)*. The Court began with the "baseline" principle that "all relevant evidence is admissible" unless excepted by the Constitution, a statute or rule and that the standard of relevance "is a liberal one." *FED.R.EVID. 402*; [*5] *Daubert, 509 U.S. at 585-589, 113 S.Ct. at 2793-94*. The Court found

that *Rule 702* [1] obliges the trial judge to act as a "gatekeeper" and screen scientific evidence for reliability and relevance. *FED.R.EVID. 702*; *Daubert, 509 U.S. at 595, 113 S.Ct. at 2798*. Regarding reliability, the Court said: "the subject of an expert's testimony must be 'scientific . . . knowledge.' The adjective 'scientific' implies a grounding in the methods and procedures of science. Similarly, the word 'knowledge' connotes more than subjective belief or unsupported speculation." *Daubert, 509 U.S. at 589-590, 113 S.Ct. at 2795*.

The Court suggested several factors in determining reliability. Of [*6] particular importance is whether "the theory or technique . . . can be (and has been) tested." *Daubert, 509 U.S. at 593, 113 S.Ct. at 2796*. Another factor is whether the theory or technique has been subjected to evaluation by peer review and publication. A third factor is the known or potential rate of error in the technique and the existence and maintenance of standards governing its operation. A final consideration is whether the theory or technique has been generally accepted in the scientific community.

The Court stressed that the standard under *Rule 702* is a "flexible one." The Court emphasized also that the focus of the inquiry is "solely on principles and methodology, not on the conclusions that they generate." *Daubert, 509 U.S. at 595, 113 S.Ct. at 2797*.

The Court favored admission of evidence on the borderline. "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional, and appropriate means of attacking shaky but admissible evidence." *Daubert, 509 U.S. at 596, 113 S.Ct. at 2798*. At the same time, the Court recognized the significant difference between the "quest for truth in the courtroom and the quest [*7] for truth in the laboratory." *Daubert, 509 U.S. at 596-97, 113 S.Ct. at 2798*. Scientific inquiry must necessarily be broad and far-reaching, with the reliability of theories under continuous study and revision. Resolution of a legal dispute, on the other hand, involves binding, final judgments that cannot be based on conjecture. Consequently, there may well be "authentic insights and innovations" of science that are nonetheless inadmissible in a court of law. *Daubert, 509 U.S. at 595-99, 113 S.Ct. at 2798-2799*.

III. ADMISSIBILITY OF EXPERTS

A. Testimony of Paul Goldstein, Ph.D.

Dr. Goldstein is a toxicology and genetics expert. He has a Ph.D. in genetics from York University in Toronto. Rec. Doc. 211, Exh. A. At the time Dr. Goldstein received his Ph.D., there was no formal toxicology degree available. Rec. Doc. 211. Despite that, his research and teachings demonstrate his qualifications in toxicology. Defendant wishes to exclude him based on his lack of training in epidemiology, pharmacology and teratology and the fact that he does not have a formal degree in toxicology. Rec. Doc. 187. Dr. Goldstein, a toxicologist, has the relative expertise to opine on the toxicological effects of [*8] Paxil. He is not disqualified from rendering a causation opinion because he does not have a medical degree. *In re Fema Trailer Formaldehyde products Liability Litigation*, No. 07-1873, 2009 WL 4508546 (E.D. La. Nov. 24, 2009).

However, Dr. Goldstein's methodology does not meet the requirement for scientific knowledge under *Daubert, 509 U.S. at 589-590, 113 S.Ct. at 2795*. Dr. Goldstein bases his general causation opinion on the "Sloot Paper." Dr. Anthony Scialli

[1] A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if: (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

testified at the *Daubert* hearing. He is a physician and board certified in OB-GYN and is the director of the Reproductive Toxicology Center, which provides information to physicians and others on the effects of chemicals on reproduction. Rec. Doc. 239, pp.56-60. At the *Daubert* hearing, Dr. Scialli testified in detail regarding the Sloot Paper. He opined that Whole Embryo Cultures as described in the article are inappropriate for assessing what is a teratogen in human risk assessment. He in fact wrote a letter to the journal criticizing the article which was subsequently published as well. As a result of the article, the authors clarified that Whole Embryo Culture tests are not intended to identify teratogens. Rec. Doc. 239, pp. [*9] 77-81. Dr. Goldstein agreed that Whole Embryo Cultures are not a basis for predicting human risk. He stated that such studies are of value in generating a *hypothesis*, which he agreed was just the "first step in that process." Rec. Doc. 187, Exh. 2, depo. Goldstein, pp. 138-139.

Dr. Goldstein's causation analysis also did not meet the required level for peer review or the standard that is accepted in his professional community, and he appears to have inappropriately applied the Bradford-Hill criteria for both general and specific causation. The Bradford-Hill criteria can only be applied after a statistically significant association has been identified. Federal Judicial Center, Reference Manual on Scientific Evidence, 599, n.141 (3d. ed. 2011) ("In a number of cases, experts attempted to use these guidelines to support the existence of causation in the absence of any epidemiologic studies finding an association . . . . There may be some logic to that effort, but it does not reflect accepted epidemiologic methodology."). *See, e.g.,* Dunn v. Sandoz Pharms., 275 F. Supp. 2d 672, 678 (M.D.N.C. 2003). Here, Dr. Goldstein attempted to use the Bradford-Hill criteria to prove causation without [*10] first identifying a valid statistically significant association. He first developed a hypothesis and then attempted to use the Bradford-Hill criteria to prove it. Rec. Doc. 187, Exh. 2, depo. Goldstein, p. 103. Because there is no data showing an association between Paxil and limb defects, no association existed for Dr. Goldstein to apply the Bradford-Hill criteria. Hence, Dr. Goldstein's general causation opinion is not reliable.

The defendants offered Dr. Goldstein as an expert on general and specific causation, meaning that the plaintiffs allege Dr. Goldstein is an expert who can opine on (1) whether Paxil can cause birth defects at all and (2) whether Paxil caused the birth defects in this instance. Dr. Goldstein stated at his deposition that he no longer held the view that E.F. had a heart defect. Rec. Doc. 233, Exh. S, depo. Goldstein, pp. 131-32. Dr. Goldstein's specific causation opinion as to limb defects must be excluded because it is not based on reliable scientific analysis or evidence. Dr. Goldstein testified to specific causation based on the fact that he believes Paxil is a teratogen and he believes that if a teratogen is present "it could possibly affect the developing [*11] cells in the-either the hand limb-or hand bud . . . ." *Id.*, p. 104. However, Dr. Goldstein also conceded that he knew of no evidence in humans or animals that demonstrates that Paxil is a limb teratogen, and he does not know if it is. *Id.*, p. 114. Hence, his hypothesis is pure speculation.

The Supreme Court requires that "an expert . . . employ[] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." In re Silica Prods. Liab. Litig., 398 F. Supp. 2d 563, 639 (S.D. Tex. 2005) (*quoting* Kumho Tire Co., 526 U.S. 137, 152, 119 S. Ct. 1167, 143 L. Ed. 2d 238 (1999)). Dr. Goldstein has demonstrated that his causation analysis did not meet the required level for peer review or the standard that is accepted in his professional community.

B. Testimony of Shira Kramer, Ph.D.

Dr. Shira Kramer offers testimony on general causation such as whether a pregnant woman's

ingestion of Paxil during the first trimester of pregnancy can cause limb or heart defects. Dr. Kramer's report did not offer an opinion as to specific causation. Rec. Doc. 233, Exh. U, depo. Kramer, pp. 44-45. Dr. Kramer's general causation opinion is that (1) Paxil affects levels of [*12] serotonin in the developing embryo, and (2) this effect can cause limb defects. Rec. Doc. 233, Exh. U, depo. Kramer, pp. 74-77.

Dr. Kramer is not qualified to offer an opinion based on serotonin's impact on limb defects. While she theorizes about "perturbation of serotonin levels," *Id.*, pp. 81-86, 92-93, Dr. Kramer is an epidemiologist and is not qualified to make the reaching arguments she makes about serotonin levels during pregnancy. Indeed, she has in other litigation conceded she is not an expert in serotonin. Rec. Doc. 188, Exh. 19, p. 81. Dr. Kramer cites to numerous epidemiological studies in her report, Rec. Doc. 188, Exh. 3, p. 31-55, but admits that this literature is "more or less noncontributory" to the correlation between Paxil exposure and limb defects. Rec. Doc. 233, Exh. U, depo. Kramer, p. 117. Dr. Kramer relies on "biological plausibility and temporality" to support her hypothesis that Paxil can cause limb defects. *Id.*, p. 119. However, beyond this assertion, Dr. Kramer does not offer any articles supporting her serotonin theory. Indeed, plaintiffs' own expert pharmacologist, Dr. Joseph Hirsch, acknowledged that nothing in his review of the scientific literature indicated [*13] that Paxil administered to pregnant animals disrupts embryonic serotonin. Rec. Doc. 188, Exh. 25, p. 60.

Furthermore, Dr. Kramer's methodology does not meet the required standard. Dr. Kramer "lumps" all congenital malformations together to make her analysis. Rec. Doc. 188, Exh. 3, p. 30. This technique is not generally accepted by the scientific community and is unreliable. *Chambers v. Exxon Corp., 81 F. Supp. 2d 661 (M.D. La. 2000), aff'd, 247 F.3d 240 (5th Cir. 2001)* (unpublished). Dr. Kramer has not demonstrated by a statistically significant measure that Paxil could be a general cause of limb or heart defects if ingested during the first trimester of pregnancy. While plaintiffs contend the fact that no epidemiology exists that provides a statistically significant association between Paxil and E.F's hand malformation is excused by the "rarity of E.F.'s malformation," the law cannot leap ahead of the science. Rec. Doc. 246, p. 4. *Wells v. SmithKline Beecham Corp., 601 F.3d 375, 381 (5th Cir. 2010)*.

IV. SUMMARY JUDGMENT

A. Plaintiffs' claims under the Louisiana Products Liability Act

Under the LPLA, there is a two-pronged test for inadequate-warning claims when the learned intermediary [*14] doctrine is applicable. The plaintiff must show (1) that the defendant failed to adequately warn the physician of a risk associated with the product that was not otherwise known to the physician; and (2) that this failure to warn the physician was both a cause in fact and the proximate cause of the plaintiff's injury." *Stahl v. Novartis Pharmaceuticals Corp., 283 F.3d 254, 265-266 (5th Cir. 2002)* (*citing Willett v. Baxter Int'l Inc., 929 F.2d 1094, 1098 (5th Cir. 1991)*).

B. Standard of Review

Rule 56 of the Federal Rules of Civil Procedure states: "The Court shall grant summary judgment if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." *FED.R.CIV.P. 56*. When considering whether any genuine issues of material fact exists, courts view the evidence and inferences drawn from that evidence in the light most favorable to the non-moving party. *United States ex re. United States ex rel. Reagan v. E. Tex. Med. Ctr. Reg'l Healthcare Sys., 384 F.3d 168, 173 (5th Cir. 2004)* (*citing Daniels v. City of Arlington, Texas, 246 F.3d 500, 502 (5th Cir. 2001)*).

An issue is material if its resolution could affect the outcome of the [*15] action. Wyatt v. Hunt Plywood Co., Inc., 297 F.3d 405, 409 (5th Cir. 2002) (citing Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1986)). A factual dispute precludes summary judgment if the evidence would permit a reasonable jury to return a verdict for the nonmoving party. Hunt v. Rapides Healthcare Sys. LLC, 277 F.3d 757, 762 (5th Cir. 2001).

The party moving for summary judgment bears the initial burden of "informing the district court of the basis for its motion, and identifying those portions of [the record] which it believes demonstrate the absence of a genuine issue of material fact." Celotex Corp. v. Catrett, 477 U.S. 317, 322, 106 S. Ct. 2548, 91 L. Ed. 2d 265 (1986). "If the moving party meets the initial burden of showing that there is no genuine issue of material fact, the burden shifts to the non-moving party to produce evidence or designate specific facts showing the existence of a genuine issue for trial." Engstrom v. First Nat'l Bank of Eagle Lake, 47 F.3d 1459, 1462 (5th Cir. 1995) (citing Celotex, 477 U.S. at 322-24). In order to satisfy its burden, the nonmoving party must put forth competent evidence and cannot rely on "unsubstantiated assertions" and "conclusory [*16] allegations." See e.g., Hopper v. Frank, 16 F.3d 92 (5th Cir. 1994); Lujan v. Nat'l Wildlife Federation, 497 U.S. 871, 871-73, 110 S. Ct. 3177, 111 L. Ed. 2d 695 (1990). The mere argued existence of a factual dispute will not defeat an otherwise properly supported motion. See Anderson v. Liberty Lobby Inc., 477 U.S. 242, 247-48, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1996). "If the evidence is merely colorable, or is not significantly probative," summary judgment is appropriate. Id. at 249-50.

C. Law and Analysis

Defendants move for summary judgment on plaintiffs claim under the LPLA on the basis that neither of Drs. Paul Goldstein nor Shira Kramer provide admissible expert testimony on general or specific causation. Rec. Doc. 233, p. 2. Therefore, defendants argue that plaintiffs have failed to establish the effect of Paxil on E.F. during Mrs. Frischhertz' pregnancy. *Id.*

Under Louisiana jurisprudence, the plaintiff in a personal injury suit, including suits under the LPLA, bears the burden of proving by a preponderance of the evidence that there was a causal relationship between his or her injury and the accident or use of the product. Maranto v. Goodyear Tire & Rubber Co., 650 So.2d 757, 759 (La.2/20/95). The test for determining the causal relationship between [*17] the accident and subsequent injury is whether the plaintiff proved through medical testimony that it is more probable than not that the subsequent injuries were caused by the accident. *Id.*

Proof of causation has two components, general and specific. *See* Pick v. American Medical Systems, Inc., 958 F. Supp. 1151, 1164 (E.D. La. 1997); Kemp v. Metabolife International, Inc., No. 00-3513, 2004 U.S. Dist. LEXIS 18738, 2004 WL 2095618 (E.D. La. Sept. 13, 2004). General causation deals with whether the substance at issue can cause diseases or disorders in people in general. Pick, 958 F. Supp. at 1164. Specific causation focuses upon whether the substance was in fact the cause of the ailments or symptoms in the particular patient. *Id.* An inability to establish specific causation is fatal to plaintiffs' claim. Id. at 1163.

Plaintiffs respond to defendant's argument that summary judgment should be granted in favor of defendants based on plaintiffs' inability to establish specific causation in one paragraph. Rec. Doc. 244, p. 20. Plaintiffs submit that their experts should be permitted to testify as explained in their opposition to the four motions to exclude testimony, but plaintiffs do not address the merits of the argument. [*18] *Id.*

Plaintiffs needed both specific and general causation testimony to meet their burden of proof. Dr. Kramer offered testimony on general causation. Rec. Doc. 233, Exh. U, depo. Kramer, pp. 44-45. Her opinion did not pass the *Daubert* test and must be excluded. Dr. Goldstein also offered testimony on general causation. Rec. Doc. 233, Exh. S, depo Goldstein. Of plaintiffs' experts, only Dr. Goldstein's testimony provided an opinion on specific causation. [2] *Id.* In particular, he needed to offer an opinion on whether Mrs. Frischhertz' alleged ingestion of Paxil while pregnant caused E.F.'s limb and alleged heart deformities. Dr. Goldstein's testimony has been excluded. Because the Court has excluded the testimony of Drs. Paul Goldstein and Shira Kramer, the plaintiffs have no expert testimony establishing general or specific causation and cannot meet their burden of establishing either general or specific causation from the ingestion of Paxil for the alleged birth defects under the LPLA.

The Court refrains from re-addressing Mrs. Frischhertz' prescribing physician, Dr. Kongara's testimony and its significance under the learned intermediary doctrine because it finds that the plaintiffs cannot establish specific or general causation. Rec. Doc. 233.

Accordingly,

IT IS ORDERED that defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Paul Goldstein, Ph.D. is GRANTED. Rec. Doc. 187

IT IS FURTHER ORDERED that defendant GlaxoSmithKline LLC's Motion to Exclude the Testimony of Shira Kramer is GRANTED. Rec. Doc. 188.

IT IS FURTHER ORDERED that summary judgment on Louisiana Products Liability Act claim is GRANTED in favor of the defendant and against the plaintiffs. Rec. Doc. 233.

IT IS FURTHER ORDERED, considering that plaintiffs have conceded that all other claims are dismissed and the Court having granted this motion for summary judgment, that judgment be ENTERED in this matter dismissing all of plaintiffs' claims with prejudice. Rec. Doc. 159.

New Orleans, Louisiana, this 21st Day of December, 2012.

/s/ Helen G. Berrigan

HELEN G. BERRIGAN

UNITED STATES DISTRICT JUDGE

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[2] Additionally, Dr. Goldstein's testimony was only related to specific causation on E.F.'s limb defect and not on his alleged congenital heart defect. Dr. Goldstein testified that E.F. did not have a congenital [*19] heart defect.